A Clinical Study of the Use of Human Chorionic Gonadotrophin in Weight Reduction

Roy Miller
Lawrence J. Schneiderman, MD
La Jolla, California

Treatment of obesity with human chorionic gonadotrophin was shown to be of no better value than saline in a double-blind crossover study of weight reduction in obese subjects. There was also no significant difference in mood, hunger, or missed injections, and no apparent difference in adherence to diet when the two agents were compared. In contrast, a significant difference was found in the ability of subjects to lose weight in the first four weeks of the study in contrast with the second four weeks, no matter which agent was used. Thus, the initiation of a new therapeutic program, even using an inert agent, has a temporary benefit – a manifestation both of placebo effect and the Hawthorne effect.

In 1954, Simeons proposed the use of human chorionic gonadotrophin (HCG) in the treatment of obesity.[1] He suggested that this hormone caused the selective loss of "abnormal fat," and enabled the obese individual to adhere to a 500 Cal diet without the usual feelings of extreme hunger.[2] Since then, this regimen has enjoyed widespread publicity and popularity.

Only a few double-blind studies of this treatment were published, and most of these failed to substantiate the usefulness of HCG.[3,4] Despite this, the method continues to have its supporters who, often basing their enthusiasm on uncontrolled clinical experience, argued that the negative studies failed to closely follow Simeons' weight loss program.[5] Asher and Harper, in a double-blind study that investigated not only weight loss but also mood and hunger, concluded that HCG is effective.[6] However, this study was criticized by Hirsch and Van Itallie who showed that a different conclusion can be drawn from the data, ie, that the beneficial results correlated best with a number of injections received, whatever the agent.[7]

A problem common to all the above studies has been the difficulty of comparing the HCG group with a control group when so many variables are involved, including degree of obesity, living conditions, interpretation of diet, and food habits. In this study these variables are minimized by using a double-blind crossover method which allows us to compare each patient to himself under the two study conditions, HCG and placebo.[8] (See Figure 1.)

From the Department of Community Medicine, School of Medicine, University of California, San Diego. Requests for reprints should be addressed to Dr. L.J. Schneiderman, Department of Community Medicine, School of Medicine S-004, University of California, San Diego; La Jolla, Calif 92093.

Study Procedure

Subjects were obese adults who presented to a rural family practice clinic requesting HCG injections for weight loss. They were offered the opportunity to take part in an eight-week study with the understanding that they would sometimes receive HCG and sometimes a placebo, but that by the end of the study they would all have received a full course of HCG treatment. The study was explained both orally and in writing and each subject signed a consent form. Patients were given an initial medical examination by the physicians who explained the weight loss regimen. No subject who had received HCG in the previous 12 months was admitted to the study. The subjects were given a written diet description which outlined a 500 Cal daily diet in the exchange manner described by Simeons, which does not include actual calorie counting. They were also given an eight-week supply of multivitamins. The subjects were then divided by random numbers into two groups, one receiving HCG for the first four-week period and sterile saline the second four-week period; the other group receiving sterile saline first, then HCG. The eight weeks commenced for each subject on the day he or she presented.

Identical appearing vials containing HCG and sterile saline were prepared and coded by the investigators. The actual content of each vial was unknown to any person in the clinic. For each subject, injections were drawn from a coded vial, a different vial each week. This assured that clinic personnel and subjects remained unaware not only of what substance was being injected, but also when the substance was changed. The injections consisted of either 125 IU HCG (0.5 cc) or 0.5 cc saline containing the same buffers as the HCG solution.

At the time the patients received their daily intramuscular injections they were asked about adherence to the diet and were also asked to rate themselves for hunger and mood on a seven-point scale (Figure 2). Subjects were weighed weekly and any missed injections were noted.

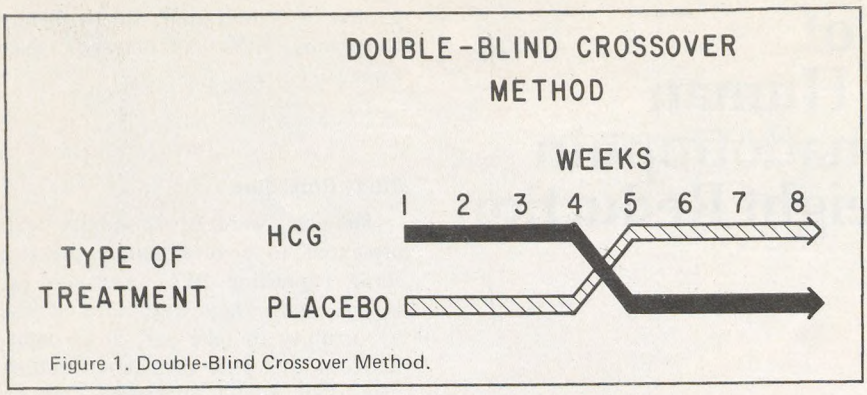

Figure 1. Double-Blind Crossover Method.

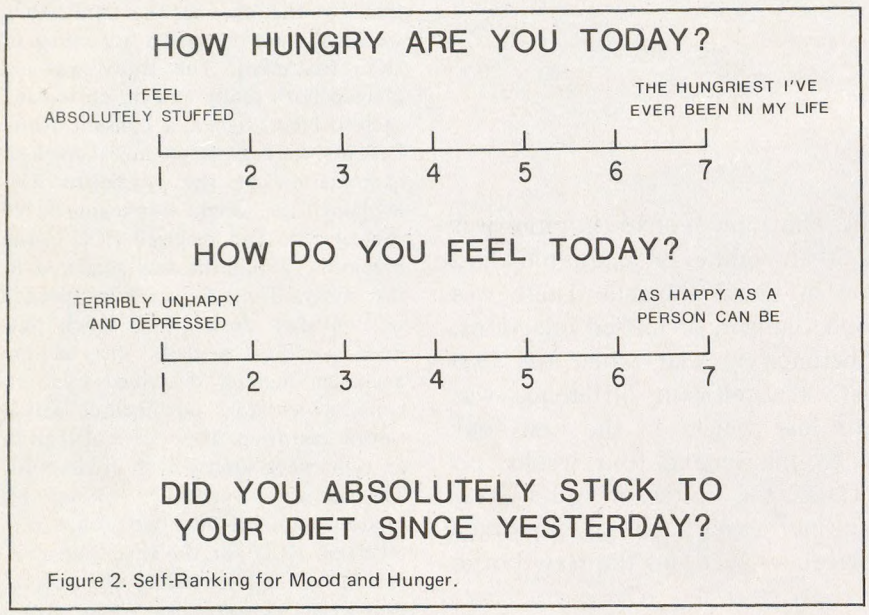

Figure 2. Self-Ranking for Mood and Hunger.

Data recorded included weight, hunger rating, mood rating, number of days deviated from diet, and number of missed injections. For each measurement an average value for each four-week period was calculated and the difference between the two values was determined for each patient who completed the eight-week course. The differences were then analyzed using the one-tail signed rank test[9] in two manners: (1) comparing values obtained during the period on HCG and the period on saline, and (2) comparing values obtained between the first and second four-week periods, regardless of the agent injected. Thus, comparisons are made on the same patient during different time periods and not between different groups of patients.

Results (See Table 1.)

Nineteen subjects (15 females and four males) took part in the study, nine starting on HCG and ten starting on the saline placebo. Eight subjects completed the eight-week course of diet and injections. Of the 11 who did not finish, five quit while receiving HCG and six while receiving the saline. Seven quit during the first four-week period and four during the second four weeks.

Discrepancies between the claimed compliance with the 500 Cal diet and the actual weight loss (or gain) observed each week on many patients made it obvious that we were not receiving accurate information from the patients on this part of the study, and it was therefore disregarded in the analysis.

Data for the eight subjects who finished was analyzed in the manner described above with the following results (Table 2).

Comparison of the HCG period with the saline period (regardless of which was first for the particular subject) showed no difference in weight loss, number of missed injections, mood, or hunger ($p>0.05$). In contrast, comparison of the first four-week period to the second showed a significant decrease in weight loss and significant increase in the number of missed injections during the second four weeks regardless of the patients injected ($p<0.01$). No significant difference was seen in the self-rankings for mood or hunger.

Discussion

It is apparent from this study that the presence of HCG in the injection given obese subjects did not contribute toward their weight loss, nor did it make the necessary caloric restrictions more tolerable. Instead, it was the initiation of a new therapy which provided the only significant – if transitory – benefit, an effect sufficiently powerful to be evident even in this small sample. This study therefore demonstrates not only the well-known placebo effect but also the Hawthorne effect.[10] Investigators at the Hawthorne Works of the Western Electric Company in Chicago, seeking to find what factors led to increases in productivity, discovered that output was enhanced by any change in routine. These investigators discovered that subjects increase their attempts to achieve goals not as a result of any specific factors, but rather as a response to the expression of personal interest in their problems, through the establishment of goal-oriented relationships, and in response to novelty itself. This phenomenon probably accounts for much of the therapeutic benefit attributed to such questionable agents as HCG.

Another noteworthy observation is that even among highly motivated obese individuals who presented requesting HCG to help lose weight, who in no way were coerced into starting the 500 Cal diet regimen, and who were being treated by their regular family physician in his office, the drop-

Table 1. Results for All Subjects

Patient number	Starting drug	Starting weight (lbs)	Sex	Age	Height (inches)	Hunger rating	Mood rating	Diet deviations/wk	Missed injections/wk	Weight loss/wk (pounds)	Hunger	Mood	Diet deviations/wk	Missed injections/wk	Weight loss/wk	Total weight loss
* 1	HCG	141-3/4	F	52	60	2.1	5.1	0	0	1.9	3.2	4.5	0.3	0.5	0.6	10
5		157-1/2	F	44	65-1/2	3.3	3.2	0.5	1	2.3						7
7		161-1/2	M	21	66	2.0	7.0	0	0.5	3.3						7
8		219	M	32	72	4.0	5.0	0	0.3	2.6						8
9		156-1/4	F	31	66-1/2	4.0	4.6	0.3	0.8	3.7	4.0	4.0	0	1.0	3.5	18
15		193	F	31	66	3.3	5.2	0.3	1.5	3.0	5.0	4.0	2.0	3.0	−4.5	8
19		182-3/4	F	31	65	5.2	5.8	0	0.5	3.7	2.3	6.0	1.0	2.0	0	15
*21		151	F			3.8	5.1	0.5	0.5	2.9	2.1	5.8	0.5	1.3	1.1	16
*30		257	F	45	65-1/2	3.4	5.7	0.5	0.3	3.7	3.1	6.0	0.3	2.0	1.5	21
* 2	P	196-3/4	F	27	67-1/2	2.8	4.4	0	0.8	4.2	1.1	7.0	0.3	2.3	0	17
* 3		201	M	49	67-1/2	3.6	4.1	0.3	0	3.0	4.1	3.9	1.5	0	2	20
* 6		251-1/2	M	31	69	3.3	5.9	0	0	6.6	3.2	6	0.5	1	4.3	44
*10		201	F	46	61-1/2	4.2	4.1	0	0	3.1	3.3	3.4	0.8	0.3	1	16
11		162	F	21	64-1/2	2.7	6.2	0	0.7	0.6						2
13		150	F			3.6	5.6	1	2.3	1.5						5
18		189-1/4	F	47		2.6	4.7	1	0	1.8						4
*22		177-1/2	F	54		3.3	3.9	0.3	0.3	3	3.3	4.5	1.3	1.3	−0.8	10
24		146-1/2	F	20	62	3.8	6.0	1	0	0.8						2
29		196	F	37	63	4.2	3.6	1.8	0.8	1.1	4.0	3.8	1	0	0.8	7
						1st 4 Weeks					2nd 4 Weeks					

Numbers are averages for each 4-week period or any completed portion. *Patients who completed full 8-week course

Table 2.
Differences Between Values for First and Second Four-Week Periods for the Eight Finishers

(Value for First Period Minus Value for Second Period)

No.	Starting drug	Hunger	Mood	Diet deviations / wk	Missed injections / wk	Weight loss / wk
1	HCG	−1.1	0.6	−0.3	−0.5	1.3
21	↓	1.7	−0.7	0	−0.8	1.8
30	↓	0.3	−0.3	0.2	−1.7	2.2
2	P	1.7	−2.6	−0.3	−1.5	4.2
3	↓	−0.5	0.2	−1.2	0	1.2
6	↓	0.1	−0.1	−0.5	−1.0	2.3
10	↓	0.9	0.7	−0.8	−0.3	2.1
22	↓	0	−0.6	−1	−1	3.8

To compare HCG to placebo period simply reverse sign of all values of patients 2, 3, 6, 10, and 22.

out rate was over half. Even among the finishers there was a significant decrease in weight loss and an increase in missed injections during the second four weeks. This lack of perseverance points out the great difficulty in getting overweight individuals to reduce. Another problem demonstrated in this short-term weight loss study is the fact that many individuals who do successfully reduce their weight through some special limited-time diet are not able to keep from regaining the lost weight. One of the few studies with a long-term follow-up indicated that 85 percent of lost weight after dieting was regained within five years.[11] Similarly, in our study several potential subjects were turned down because they had already completed a "successful" course of HCG within the preceding 12 months, yet were presenting with the same original weight as they did for their first course.

The treatment of obesity is notorious for the number of fads which come and go, and the recent history of HCG indicates that this regimen will probably be no different. Serious weight reduction requires long-term changes in overall eating habits, even in life-styles. We are still searching for the most effective way of helping patients who wish to reduce.

Acknowledgement

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Caution, very close observation, and careful adjustment of dose are necessary when: insulin is withdrawn during the trial period in order to avoid ketosis, acidosis, and coma; thiazide diuretics are administered which may result in aggravation of diabetic state and increased tolbutamide requirement, temporary loss of control, or even secondary failure; treating patients with impaired hepatic and/or renal function and debilitated, malnourished, or semistarved patients in order to avoid severe hypoglycemia which may require corrective therapy over several days; and treating patients with severe trauma, infection, or surgical procedures where temporary return to insulin or addition of insulin may be necessary. Response to tolbutamide is diminished in patients receiving therapy with beta-blocking agents.

As some diabetics are not suitable candidates, it is essential that the physician familiarize himself with the indications, limits of application, and selection of patients for therapy.

Patients must be under continuous medical supervision, and during the initial test period should communicate with the physician daily, and during the first month report at least once weekly for physical examination and definitive evaluation. After a month, examinations are recommended monthly or as indicated. Appearance of ketonuria, increase in glycosuria, unsatisfactory lowering of persistent elevation of blood sugar, or failure to obtain and hold clinical improvement indicate non-responsiveness to

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It may well be that using obesity as a criterion of hypothyroidism warps the figures. Certainly, only a very small percentage are confirmed by TSH. Those I would accept as valid.

There is perhaps no more widespread fallacy in all of medicine than the assumption that obesity relates to hypothyroidism. If this article promotes that idea, it is likely to have an adverse influence on patient care.

J. Blair Pace, MD
Associate Clinical Professor
Department of Family Medicine
University of California
Irvine

Resident Evaluation

To the Editor:

Dr. Corley's discussion (*Corley JB: In-training residency evaluation. J Fam Pract 3:499-504, 1976*) regarding resident evaluation deserves comment, for I believe that much remains as conjecture, rather than proven fact.

I submit that the opening comment on a lack of evaluation in residency training may no longer be true. As part of a recent assessment project, I learned that 15 out of 17 randomly selected residencies in family medicine across the country used some tool, however imperfect, for resident evaluation.

Secondly, I submit the evaluation process may do wonders for the faculty, but I have yet to see proof of its decided advantage to each resident. I say this despite my personal conviction to the contrary, and my professional use of a system quite similar to that proposed by Dr. Corley. Proof of efficacy, however, seems lacking.

Third, and perhaps most important, the systems we develop in our graduate programs in family medicine should be tailored to the advantages of all programs who train the family doctor. I fear the time and faculty required by the written proposal would exceed the budget of the common residency program.

I plead, therefore, for further evaluation of evaluation, with all due respect to my learned friend, the author.

John E. Donnelly, MD
University of Connecticut
Farmington

The above letter was referred to Dr. Corley who replies as follows:

Dr. Donnelly's point is well taken as to the lack of any definitive research in medical education to substantiate the hypothesis that evaluation of learning does, in truth, promote the acquisition of professional competence. A plethora of research in educational psychology gives reasonable evidence that the hypothesis probably is sound, yet it may be true that tomorrow's task should be the evaluation of residency evaluation itself, if only as to the legitimate problem of cost effectiveness.

Dr. Donnelly has also accurately reported that most residencies in family practice do engage in some form of resident evaluation. Nevertheless, it has been accurately stated by Blaine Worthen and others that while verbal statements and token programs of evaluation are abundant, *genuine* evaluations of educational programs are distressingly rare.

All graduate training programs suffer from a restrictive limitation of resources – financial, time, and faculty. But surely it remains unrealistic to launch innovative residency programs in family practice if no plan exists to evaluate these exciting innovations. Each residency must decide for itself how best to spend its time and funds. My plea remains not to neglect evaluation. Without evaluating resident progress, how may a program be reasonably confident that its limited resources are being wisely invested? Evaluation programs need not be all embracing or extravagantly ambitious. They can be initiated in modest increments. But, to be effective, they do require as a minimum, "that a conceptual philosophy, a rational plan of implementation, and an acceptable administration" be thoughtfully defined prior to deployment.

John B. Corley, MD
Medical University of South Carolina
Charleston